

Nuclear receptor TLX stimulates hippocampal neurogenesis and enhances learning and memory in a transgenic mouse model.

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Authors: Kiyohito Murai, Qiu hao Qu, GuoQiang Sun, Peng Ye, Wendong Li, Grace Asuelime, Emily Sun, Guochuan E Tsai, Yanhong Shi

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Public Summary:

The role of the nuclear receptor TLX in hippocampal neurogenesis and cognition has just begun to be explored. In this study, we generated a mouse model that expresses TLX under the control of a neural precursor marker nestin. Transgenic TLX expression led to enlarged brains with bigger hippocampal dentate gyrus and increased numbers of newborn neurons. Specific expression of TLX in adult hippocampal dentate gyrus, a brain region that is important for learning and memory, increased the numbers of proliferating neural progenitors and newborn neurons. Furthermore, the neural precursor-specific expression of the TLX transgene substantially rescued the neurogenic defects of mice with a deletion of the TLX gene. Consistent with increased neurogenesis in the hippocampus, the TLX transgenic mice exhibited enhanced cognition with increased learning and memory. These results suggest significant contributions of TLX to hippocampal neurogenesis, learning, and memory.

Scientific Abstract:

The role of the nuclear receptor TLX in hippocampal neurogenesis and cognition has just begun to be explored. In this study, we generated a transgenic mouse model that expresses TLX under the control of the promoter of nestin, a neural precursor marker. Transgenic TLX expression led to mice with enlarged brains with an elongated hippocampal dentate gyrus and increased numbers of newborn neurons. Specific expression of TLX in adult hippocampal dentate gyrus via lentiviral transduction increased the numbers of BrdU⁺ cells and BrdU⁺NeuN⁺ neurons. Furthermore, the neural precursor-specific expression of the TLX transgene substantially rescued the neurogenic defects of TLX-null mice. Consistent with increased neurogenesis in the hippocampus, the TLX transgenic mice exhibited enhanced cognition with increased learning and memory. These results suggest a strong association between hippocampal neurogenesis and cognition, as well as significant contributions of TLX to hippocampal neurogenesis, learning, and memory.

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